21. The method according to claim 20, wherein said adipose tissue is reduced from its original volume by at least 25%.

REMARKS

With the filing of this amendment, claims 1-21 are pending in the application. These include claim 19 submitted in AMENDMENT B--AFTER FINAL, amended claims 1 and 16 submitted in AMENDMENT C--AFTER FINAL, and claim 20 submitted in PRELIMINARY AMENDMENT D.

Rejection of the claims under 35 U.S.C. §103 as being unpatentable over Lee et al., combined with Guidicelli et al., is respectfully traversed.

Applicants' invention provides what can be called "chemical liposuction." The amount of adipose tissue at selected locations in the body is reduced for cosmetic purposes by introducing into said adipose tissue collagenase, or collagenase plus another proteinase. As recited in amended claims 1 and 16 and in claim 20 (all other claims are dependent), the adipose tissue comprises connective tissue and fat, the collagenase digests/dissolves the connective tissue, and fat thus released from the adipose tissue is

removed/metabolized by the body, leaving the selected location with a reduced amount of adipose tissue. Claims 19 and 21 recite that the reduction from original volume is from 25% to 75% (claim 19) or at least 25% (claim 21).

Lee et al., on the other hand, are not interested in bodily adipose tissue except as the raw material source of microvessel cells used to coat implants such as artificial blood vessels and prosthetic devices. Adipose tissue obtained by liposuction is subjected in the laboratory to the action of collagenase plus chymopapain. The collagenase digests the connective tissue, releasing the microvessel cells and adipocytes (fat cells). Upon centrifuging, the former formed a pellet; adipocytes and liquid supernatant were pipetted off. Lee et al. also state that their enzyme mixture can be used to digest connective tissue in vivo for the treatment of several diseases--none of which involves adipose tissue.

There is nothing whatsoever in Lee et al. to make obvious or predictable that their enzymes could be used to digest the connective tissue of adipose tissue in vivo or what would happen to released fat. In applicants' invention the body itself removes released fat from the selected

location of treatment, resulting in less fatty material there. Original volume can be reduced by at least 25% (see specification, page 2, lines 17-19; cf. Experiment E at page 15 for weight losses of 41%, 25% and 18%, the average being 28%). This disappearance of fat from the selected locations provides the desired cosmetic result. It could not be predicted from Lee et al.

Throughout the voluminous Lee et al. disclosure, only the words "digest" and "hydrolyze" are used; nothing is said about reducing the amount of anything. In applicants' disclosure are: "reducing the amount", "dissociation and reduction of adipose tissue"; "rid patient of unwanted subcutaneous fat cells"; "reduction of sub-cutaneous fat"; "freeing of fat from adipose tissue."

Lee et al. disclose the in vitro treatment of adipose tissue obtained by liposuction. Though they state (col. 7, line 60 to col. 8, line 7) that their collagenase plus chymopapain can be utilized to digest connective tissue and administered in vivo for the treatment of certain maladies, this in no way suggests that the body will carry away the principal component of the treated tissues. This is an unobvious result in applicants' method.

The rejection is not strengthened by Guidicelli et al., who isolate adipocytes for further experimentation by digesting adipose tissue with collagenase and with collagenase plus trypsin.

Lee et al. teach only digesting the connective tissue matrix. They teach nothing about digesting the entire tissue, and one of ordinary skill in the art would not expect that in vivo use of the enzymes would cause the cells released from the matrix to be digested or dissolved. In fact, Lee et al. teach that both adipocytes and microvessel cells survived the enzyme treatment. There is no reason to predict that contacting in vivo adipose tissue with collagenase would result in loss of any components of the adipose tissue other than the connective tissue matrix, nor what the body would do with free adipocytes and free fat. Thus, applicants' cosmetic result which requires the disappearance of fat from the selected location is unobvious and patentable.

It is noteworthy that Lee et al. mentioned administration of their enzymes to a human or animal for the treatment of seven conditions, but did not include reducing the amount of subcutaneous fat. They actually carried out

surgical liposuction to obtain adipose tissue, yet the idea of "chemical liposuction," as taught and claimed by applicants, did not occur to them. Nor did it occur to the large number of investigators who over the past 30 years have utilized collagenase for a great variety of purposes. Nor did it occur to those working in the field of liposuction, that has greatly expanded over the past 15 years, despite the ready availability of collagenase and its in vivo use for other purposes.

A 1989 article in Clinics in Plastic Surgery, Vol. 16, No. 2, pp. 385-394, reported 11 deaths and 9 cases of serious morbidity per 100,000 suction lipectomies. A 1991 article in Plastic and Reconstructive Surgery, Vol. 88, No. 2, pp. 239-246, reported 3 serious complications from suction lipoplasty in 3,511 cases, a frequency of 85 per 100,000. Even since the date of the present Office Action, another death has been reported in the press. The rapidly increasing number of procedures performed annually and the serious complication and mortality/morbidity statistics eloquently point to the need for an alternative procedure to liposuction and the unobviousness of applicants' invention.

Allowance is courteously solicited.

The Examiner is respectfully requested to telephone applicants' attorney at the number listed at the foot hereof, if there are questions or issues regarding allowance.

Respectfully submitted,

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Certification under 37 CFR 1.8(a): I hereby certify that this correspondence is being deposited with the United States Postal Service as first-class mail in an envelope addressed to Commissioner of Patents and Trademarks, Washington, DC 20231 on JUL 19 1997.

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